REMARKS

a. Information Disclosure Statement

Enclosed is a full copy of the Sepaniak reference, along with an Information Disclosure Statement and Form PTO 1449. Applicant respectfully requests consideration of this reference and indication of such in the record.

b. Formal Rejections

While Applicant disagrees with the Examiner's objection to the prior amendment to the specification, Applicant amended the specification to remove the text previous added by amendment.

In response to the rejection of the specification and claims based on 35 USC 112, first and second paragraphs, Applicant amended claims 1 and 16 to recite reference to the exit of the separation channel, rather than to a "transition" which the Examiner's took issue with. Applicant submits that these amendments are supported by the original specification as filed, and introduce no new matter.

Referring to page 16, line 18 to page 17, line 5, it has been disclosed that as the analytes flow from the separation channel 504 of capillary column 22 into the collar 10, the analytes remain subject to the applied potential. As a result, the analytes continue to maintain separation state (i.e., in the form of a series of separate analyte bands) as they migrate/flow past the detection zone 20. Some mixing or diffusion of the analytes may occur in the collar near the exit of the separation channel 504, but analytes "regroup" into separated state as they continue down along the collar 10 (i.e., the detection section recited in claim 1 and 30) towards the detection zone 20. The detection zone 20 is preferably located at 100-500 x ID of the collar 10, more like

225 times the ID, to provide sufficient distance for the analytes to regroup before detection at the detection zone 20. Because the diameter of the detection zone is larger than the diameter of the separation channel 504, the analyte bands are narrower in the axial direction. Thus the detection resolution may be improved as a result.

Further, referring to the embodiment of Fig. 13, which clearly shows the flow from the narrower separation channel into the wider detection section. This embodiment clearly shows in no indefinite way the exit of the separation channel. This is the case with Fig. 13, as is also the case with Fig. 9B and Fig. 10B.

When viewed as a whole, Applicant respectfully submits that the "exit of the separation channel" is well defined in the specification to provide support to the claims pursuant to the requirements of the first paragraph of 35 USC 112, and reference to such in the claims would be definite, under the second paragraphs of 35 USC 112.

c. Claim Rejections – 35 USC §103

1. Zhu

Independent claims 1 and 16 were rejected by the Examiner as being unpatentable in view of U.S. Patent No. 5,763,277 to Zhu, and separately in view of U.S. Patent No. 5,650,846 to Yin. These rejections are respectfully traversed.

Zhu does not teach or suggest that the detection zone could or should be located at a distance 100 to 500 times of the width of the wider detection section, from the exit of the narrower separation channel, as required by the independent claims 1 and 16 as amended.

In fact, Zhu is silent in its written disclosure as to the location of the detection zone, much less disclose defining the detection zone to be at such a distance from the transition. Since there is no accompanying disclosure of the location of the tip of the fiber optic 3, one can and should only refer to what is specifically shown in the drawings in Zhu. Fig. 3 in Zhu shows the fiber optic 3 inserted into the increased inner diameter 1d of the bore 2, with the tip within 1 time of the increased diameter 1d from the transition from the smaller diameter. Fig. 3 does not specifically or by implication show the tip to be at the recited distance in claims 1 and 30 as amended. Zhu did not address the concerns of mixing, diffusion and regrouping of analyte back into separated state, and accordingly Zhu would not have disclosed the specific location of the detection zone, without consideration of mixing, diffusion and regrouping of analytes.

Further, the location of the detection zone at the specific recited distance is not an obvious matter of design choice, since the motivation for such (e.g., to take into account of analyte mixing, diffusion and regrouping) is not found anywhere in Zhu. These considerations are beyond routine experimentation to determine optimum values. Without the teaching of the present invention, one skilled in the art would not know what conditions or parameters to optimize and what considerations to be taken into account to optimize such parameters and conditions, let alone how to optimize such parameters and conditions.

Claim 1 has been amended to require that "mixing or diffusion of analytes occurs near the exit of the separation channel; ... a detector system detecting radiation emission axially from a location along the detection section defining a detection zone as analytes pass the detection zone, said location being defined at a distance of 100 to 500 times the second width of the detection section from the exit of the separation channel, thereby allowing analytes sufficient distance to regroup from the mixing or diffusion near the exit of the separation channel, said

detector system including an optic fiber having an end in close proximity to the detection zone". Claim 16 has been amended in similar fashion.

In fact, Zhu teaches away from the present invention defined in claims 1 and 16. For example, concerning the issues of analyte mixing, diffusion and regrouping, Zhu does not even need to address these issues by simply placing the end of the optical fiber within 1 time of the increased diameter 1d from the transition from the smaller diameter. By having the detection fiber end close to the transition, there would be significantly less opportunity for analyte mixing and diffusion, and hence regrouping at a significant distance from the transition is not needed.

Applicant respectfully submits that Zhu is complete and functional in itself, so there would be no reason to modify Zhu in the manner suggested only by the Examiner. Given that Zhu chose to place the end of the optical fiber close to the transition, it does not make sense to modify Zhu to have the end of the optical fiber at a significantly different distance from the transition. Any such modification of Zhu would frustrate its intended purpose. It is clear that Zhu and the present invention take mutually exclusive paths and reach different solutions for analyte detection. Consequently, Zhu teaches away (expressly or by implication) from the present invention. It would not be logical to modify Zhu to obtain the present invention.

Applicant respectfully submits that the Examiner have read and/or applied the cited cases out of context. Zhu is completely silent on the conditions or parameters to be taken into considerations for optimization. There are many conditions and parameters that should be taken into considerations (e.g., mixing, diffusion, regrouping, diameter of detection zone, etc.). Without any reference or discussion to any of these parameters and considerations, Zhu does not disclose "the general conditions of a claim ... disclosed in the prior art", or what range of variables that should be optimized! To find Zhu to render obvious the structure recited in claims

1 and 16 as suggested only by the Examiner, would necessarily require impermissible hindsight reconstruction made possible only by the disclosure of the present invention.

Further, the Examiner appeared to have taken judicial notice to support his conclusion that one of ordinary skill in the art would vary the distance of the detection zone for optimization purposes. Applicant respectfully objects to such judicial notice, and requests that the Examiner specifically identifies references that provide such support, which the Examiner is obligated to provide under the MPEP.

Accordingly, Zhu would not have rendered obvious the present invention defined in claims 1 and 16. All the dependent claims would likewise be non-obvious over Zhu.

2. Yin

Yin shares similar deficiencies as noted above for Zhu.

Further, Yin discloses the use of a "flare" for receiving the interfacing end of the optical fiber, thereby facilitating the alignment and nonfixed confinement of the interfacing end of the optical fiber. As used in Yin, non-fixed coupling between an end of a microcolumn and an end of an optical fiber refers to the positioning and maintaining the position of these ends relative to each other in close proximity without rigidly affixing any of these ends to any mechanical structure (see column 4, lines 29+). Close proximity is for the purpose of preventing "excessive loss of light around the interfacing end 30 of the optical fiber yet large enough to not hinder fluid from exiting the micro-column. For example, this distance (i.e., the gap) can be from about 0.2 to 0.5 of the outside diameter of the smaller of the microcolumn 12 and the optical fiber 14". (See column 5, line 34+.) As in the case for Zhu, the tip of the optical fiber is to be within less than one time the increased diameter of the flare from the transition from the smaller diameter

section, not a widened section that extends to over 500 times the width of the widened opening from the exit of the narrower section (separation channel).

Further, the structure of the detection configuration in Yin dictates the close proximity o of the detection fiber end to the transition. Yin uses a larger channel 122 in Fig. 8, which is coaxial to the capillary column 124 and the optical fiber 114. There is coaxial flushing fluid flow around the capillary column124 and optical fiber 114. The analytes exit from the flare 139 of capillary column 124, into the flushing fluid flow in the larger channel 122. There would be significant analyte diffusion and mixing with the flushing fluid throughout the downstream flushing flow. Accordingly, regrouping of mixed or diffused analytes is not possible and hence not contemplated in view of the flushing fluid. Consequently, Yin is only concerned with maintaining the end of the fiber in close proximity to the flared end of the capillary column 124 to detect analytes before such mixing and diffusion occur in the flushing flow, in additional to prevent excessive loss of light at the interface. It is not concerned with, and in fact need not be concerned with regrouping of analyte mixing and diffusion.

As in the case of Zhu, applicant respectfully submits that Yin in fact teaches away from the present invention defined in claims 1 and 16. For example, concerning the issues of analyte mixing, diffusion and regrouping, Yin does not even need to address these issues by simply placing the end of the optical fiber within 1 time of the increased diameter from the transition from the smaller diameter. By having the detection fiber end close to the transition, there would be significantly less opportunity for analyte mixing and diffusion, and hence regrouping at a significant distance from the transition is not needed.

Applicant respectfully submits that Yin is complete and functional in itself, so there would be no reason to modify Yin in the manner suggested only by the Examiner. Given that

Yin chose to place the end of the optical fiber close to the transition, it does not make sense to modify Yin to have the end of the optical fiber at a significantly different distance from the transition. Any such modification of Yin would frustrate its intended purpose. It is clear that Yin and the present invention take mutually exclusive paths and reach different solutions for different problems solved (Yin deals with analytes in flushing flow which cannot be regrouped, as compared analyte regrouping in the present invention). Consequently, Yin teaches away (expressly or by implication) from the present invention. It would not be logical to modify Yin to obtain the present invention.

The other arguments presented in connection with Zhu but not specifically mentioned here are equally applicable to Yin.

Accordingly, Yin would not have rendered obvious the present invention defined in claims 1 and 16. All the dependent claims would likewise be non-obvious over Yin.

3. Other References

Given the traversal of independent claims 1 and 16 above, the further combinations of the other cited and applied references with Yin would not render the present invention obvious. The other references do not make up for the deficiencies of Yin.

For example, with respect to Taylor, it does not disclose the capillary having a widened section at the detection zone, but rather a capillary having a uniform width along its length, even at the detection zone. Furthermore, there is no motivation to combine Taylor and Yin in the first place. Yin teaches use of a fiber optic for **axial detection** and teaches only off-column excitation. Rather, Taylor discloses off-column detection. In contrast to Yin, Taylor discloses use of a fiber optic for **axial excitation** of the sample and does not disclose use of this fiber optic

for axial detection. Taylor therefore conflicts with Yin. There is no motivation found anywhere in either Taylor or Yin, if and how **axial detection** in Yin can and should be modified with teaching from a reference like Taylor that is directed to **axial excitation**. Accordingly, in fact, Yin teaches away from Taylor. Any modification of Yin based on Taylor would frustrate the objectives of Yin.

However, the Examiner indicated in the Office Action that he referred to Taylor for the teaching of specific structures recited in the dependent claims. The Examiner appears to have dissected the overall teaching of axial excitation in Taylor, and selectively and conveniently adopted certain "useful" information from such dissection, to show that such structures may be readopted for another purpose, even though Taylor effectively teaches away, expressly and by implication, from a system implementing axial detection. Consequently, the modification of Yin to selectively adopt structures in the axial excitation scheme of Taylor as suggested by the Examiner, can only be based on impermissible hindsight reconstruction made possible by the disclosure of the present invention.

Accordingly, even if Taylor can somehow be combined with Yin, the combination would not result in the present invention defined in claims 1 and 16.

Accordingly, the rejected dependent claims are patentable over Yin in view of Taylor. With respect to the dependent claims that were rejected further in view of other references, those other references do not make up for the deficiencies of Taylor noted above.

d. New Claim 22

Taylor does not disclose the capillary having a widened section at the detection zone, but rather a capillary having a uniform width along its length, even at the detection zone. Further, Taylor does not disclose the recited location of the detection zone.

e. Double Patenting Rejections

Applicant does not believe the pending claims are subject to the judicial created doctrine of double patenting with reference to Applicant's patent no. 6,529,275 and copending Patent Application No.09/887,871. However, in the interest of forwarding this case to early issuance, Applicant will consider filing a terminal disclaimer once all other outstanding prior art rejections have been overcome.

CONCLUSION

In view of all the foregoing, Applicant submits that the claims pending in this application are patentable over the references of record and are in condition for allowance. Such action at an early date is earnestly solicited.

Since two RCE's have been filed for the present application, should the Examiner not deem the present application as amended to be in condition for allowance, Applicant respectfully requests the courtesy of the Examiner to grant a telephonic interview with the undersigned representative to discuss any outstanding issues that may not have been adequately addressed in this response.

Respectfully submitted,

Dated: December 13, 2004

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